HIGH PRODUCTION VOLUME (HPV)

CHEMICALS CHALLENGE PROGRAM

TEST PLAN

For

Phosphoric acid, Dibutyl phenyl ester (DBPP)

CAS NO. 2528-36-1

Prepared by:

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EXECUTIVE SUMMARY

Solutia Inc. voluntarily submits the following screening information data and Test Plan covering the chemical, Phosphoric acid, dibutyl phenyl ester, also known as Dibutyl Phenyl Phosphate or DBPP (CAS No. 2528-36-1), for review under the Environmental Protection Agency's High Production Volume (HPV) Chemicals Challenge Program.

A substantial amount of data exists to evaluate the potential hazards associated with DBPP. Use of key studies or estimation models, available from data already developed, provide adequate support to characterize the Endpoints in the HPV Chemicals Challenge Program without the need for additional, unnecessary testing.

TABLE OF CONTENTS

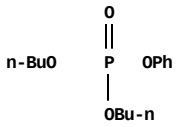
TEST PLAN FOR DIBUTYL PHENYL PHOSPHATE (DBPP)

I. INTRODUCTION AND IDENTIFICATION OF CHEMICAL

Under EPA's High Production Volume (HPV) Chemicals Challenge Program, Solutia Inc. has committed to voluntarily compile basic screening data on Dibutyl Phenyl Phosphate, also known as DBPP. The data included in this Test Plan provide physicochemical properties, environmental fate, and human and environmental effects of DBPP, as defined by the Organization for Economic Cooperation and Development (OECD). The information provided comes from existing data developed on behalf of Solutia Inc. or found in the published scientific literature and fulfills Solutia's obligation to the HPV Challenge Program.

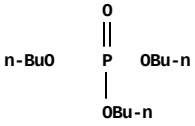
A. Structure and Nomenclature

Commerical DBPP is manufactured as what is called in the industry a "phosphate ester base stock". As such, it is actually a mixture of 3 organophosphate (OP) ester components in an approximate ratio of 70% Dibutylphenyl Phosphate (DBPP): 15% Tributyl Phosphate (TBP): 15% Butylphenyl Diphenyl Phosphate (BDPP). Following is a structural characterization of DBPP and associated esters, including their nomenclature. For the remainder of this dossier, we will refer to DBPP, recognizing we are designating the 70:15:15 OP ester mixture.

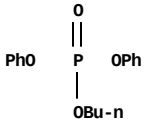


Phosphoric acid, dibutyl phenyl ester
CAS No. 2528-36-1
Synonyms: Dibutyl Phenyl Phosphate, DBPP

Additional components of commercial grade dibutylphenyl phosphate (DBPP) include:



Phosphoric acid, tributyl ester
CAS No. 126-73-8
Synonyms: TBP, tributyl phosphate



Phosphoric acid, butyl diphenyl ester
CAS No. 2752-95-6
Synonyms: butyl diphenyl phosphate, BDPP

B. Manufacturing & Use

Commercial DBPP is manufactured by a single US producer, Solutia Inc. at a single manufacturing site. The manufactured product is a phosphate ester base stock, and as such consists of the three organophosphate ester components as described in the Structure and Nomenclature section of this Test Plan. This composition is a consequence of the reaction chemistry and is not altered during manufacture. The majority of the data presented in this Test Plan has the commercial mixture as the test article.

Commercial DBPP is blended as a component with other ingredients into certain SKYDROL ® brand fire resistant Hydraulic Fluids. This blending is conducted at a single manufacturing site in a closed operation.

A TLV of 3.5 mg/m3 (8-hr TWA) has been established for DBPP (ACGIH, 2002). In addition, a second component of commercial DBPP, Tributyl Phosphate (TBP), has an established TLV of 2.2 mg/m3 (8-hr TWA)(ACGIH, 2002). These values have been established to protect against possible ocular, dermal or respiratory tract irritation. Only a few employees are involved in the manufacture and blending of commercial DBPP. There is minimal potential for skin or airborne exposure due to the closed nature of the manufacturing and blending processes. Eye and skin protection are routinely worn, and respiratory protective equipment is available should airborne exposure limits be exceeded.

SKYDROL Hydraulic Fluids are approved for use in essentially all of the world's commercial aircraft and in many types of military and general aviation aircraft. These hydraulic fluids are used in closed systems within an aircraft, thus potential for exposure to commercial DBPP by passengers is minimal. The potential for occasional, inadvertent ocular, dermal or inhalation exposure during aircraft maintenance activities has been minimized by use of good industrial hygiene practices by aircraft mechanics. Customer's employees are routinely provided with Solutia's information on the effectiveness of various types of protective equipment.

II. TEST PLAN RATIONALE

The information obtained and included to support this Test Plan has come from either 1) internal studies conducted by/or for Solutia Inc. (or its predecessor Monsanto Co.), 2) has been extracted from the scientific literature either as primary references or as found in well-accepted, peer-reviewed reference books, or 3) were estimated using environmental models accepted by the US EPA (1999b) for such purposes. This assessment includes information on physicochemical properties, environmental fate, and human and environmental effects associated with DBPP. The data used to support this program include those Endpoints identified by the US EPA (1998); key

studies have been identified for each data Endpoint and summarized in Robust Summary form and included in Section VI. of this Dossier.

All studies were reviewed and assessed for reliability according to standards specified by Klimisch *et al* (1997), as recommended by the US EPA (1999a). The following criteria were used for codification:

> 1. Reliable without Restriction - Includes studies which comply with US EPA and/or OECD-accepted testing guidelines, which were conducted using Good Laboratory Practices (GLPs) and for which test parameters are complete and well documented,
>
> 2. Reliable with Restrictions – Includes studies which were conducted according to national/international testing guidance and are well documented. May include studies conducted prior to establishment of testing standards or GLPs but meet the test parameters and data documentation of subsequent guidance; also includes studies with test parameters which are well documented and scientifically valid but vary slightly from current testing guidance. Also included were physical-chemical property data obtained from reference handbooks as well as environmental endpoint values obtained from an accepted method of estimation (i.e. EPIWIN).
>
> 3.Not Reliable – Includes studies in which there are interferences in either the study design or results that provide scientific uncertainty or where documentation is insufficient.

Those studies receiving a Klimisch rating of 1 or 2 are considered adequate to support data assessment needs in this Dossier.

III. TEST PLAN SUMMARY AND CONCLUSIONS

Conclusion: All HPV Endpoints have been satisfied with data from studies that were either well documented, used OECD guideline methods and conducted in accord with GLPs, or were estimated from acceptable estimation modeling programs. Hence, no further testing for any of the HPV Endpoints is deemed necessary, as summarized in Table 1.

In summary:
Physical-chemical property values (Melting Point, Boiling Point, Vapor Pressure, Partition Coefficient and Water Solubility) were obtained from reputable reference books, utilized accepted estimation models or are measured values which have come from acceptable studies. Thus, these values were classified as "2-Reliable with restrictions".

Environmental Fate values for Photodegradation, and Transport (Fugacity) were obtained using a computer estimation –modeling program (EPIWIN, 2002) recommended by EPA; as such, they were designated "2-Reliable with restrictions". The EPIWIN program was unable to estimate Stability in Water (Hydrolysis). Based on the lack of functional groups suggestive of the potential for hydrolysis to occur and the stability of DBPP as a test substance in dynamically conducted aquatic toxicity testing, it is accepted that DBPP does not hydrolyze in an acidic or near neutral aqueous environment. From data available, aqueous hydrolysis of DBPP can increasingly occur as alkalinity increases, a property observed with other alkyl, aryl phosphates. Thus, no additional testing is needed for further confirmation. Biodegradation testing (SCAS test) of DBPP was conducted. That study was well-documented and was conducted using methodology that proceeded, but is considered consistent with, methodology recommended in OECD test guideline 302. It, thus, has been designated as "2-Reliable with restrictions".

Ecotoxicity – An acute fish study conducted for 14 consecutive days of treatment, and thus extending OECD guidelines for Acute Toxicity to Fish (OECD 203) has been used to fulfill the Acute Fish Toxicity Endpoint. As this study was conducted according to methods which are even more rigorous than OECD guidelines for this endpoint, and as the study itself is well documented, it has been designated "1-Reliable without restrictions". Acute Plant Toxicity and the Acute Invertebrate Toxicity studies, consistent with OECD test guidance, have been designated "2-Reliable with restrictions". Additionally, chronic aquatic studies with r. trout and daphnia (both considered "1-Reliable without restriction") further support these HPV Endpoints such that no additional testing with DBPP is warranted.

Mammalian Toxicity Endpoints (Acute Toxicity, Repeated Dose Toxicity, Ames and Chromosomal Aberration Testing, and Reproductive Toxicity) have all been filled with tests that either conformed directly with OECD test guidance or followed test designs similar to OECD guidance.

The Acute Toxicity Endpoint is supported by an oral rat toxicity study which was conducted preceding codification of OECD and GLP guidance but was well documented and followed methodology consistent with later guidance; it is considered "2- Reliable with restrictions".

The Repeated Dose Toxicity Endpoint has been met with a 90-Day Subchronic rat study (similar to OECD guideline 408) conducted in accordance with GLPs. It has been codified as "1- Reliable without restrictions".

An Ames test, limited by conduct of a single rather than double trial, has been used to fulfill this HPV Endpoint. This study is considered "2-Reliable with restrictions". In support of that study and its results, we also provide a summary of a similar Ames test, conducted under the auspices of the US NTP, as Supplemental information. An *in vivo* Chromosomal Aberration assay has been used to support its respective

Endpoint. Following a study design equivalent to OECD guideline # 475, it has been classified as "1- Reliable without restriction".

The Reproductive Toxicity HPV Endpoint has been filled using a Two-Generation Rat Reproduction study which followed OECD test guideline #416 and is considered "1- Reliable without restriction".

Following is a tabular summary of the Test Plan developed for DBPP.

Table 1. Test Plan Matrix for Dibutyl Phenyl Phosphate (DBPP)

	Info. Avail.	OECD	GLP	Other Study	Estimat. Method	Accept-Able ?	Testing Recomm.
PHYSICAL CHEMICAL							
Melting Point	Y	N	N	N	Y	Y	N
Boiling Point	Y	N	N	N	-	Y	N
Vapor Pressure	Y	N	N	N	-	Y	N
Partition Coefficient	Y	N	N	N	-	Y	N
Water Solubility	Y	N	N	N	-	Y	N
ENVIRONMENTAL FATE ENDPOINTS							
Photodegradation	Y	N	N	N	Y	Y	N
Stability in Water	Y	N	N	N	-	Y	N
Biodegradation	Y	N	N	Y	-	Y	N
Transport between Environmental Compartments (Fugacity)	Y	N	N	N	Y	Y	N
ECOTOXICITY							
Acute Toxicity to Fish	Y	Y	Y	Y	-	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	N	Y	Y	-	Y	N
Toxicity to Aquatic Plants	Y	N	N	N	-	Y	N
MAMMALIAN TOXICITY							
Acute Toxicity	Y	N	N	N	-	Y	N
Repeated Dose Toxicity	Y	Y	Y	Y	-	Y	N
Genetic Toxicity – Mutation (Ames)	Y	N	N	Y	-	Y	N
Genetic Toxicity – Chromosomal	Y	Y	Y	N	-	Y	N

Chromosomal Aberrations							
Developmental Toxicity	-	-	-	-	-	-	-
Reproductive Toxicity	Y	Y	Y	N	-	Y	N

Y = Yes; N = No; - = Not applicable

IV. DATA SET SUMMARY AND EVALUATION

The key studies used in this assessment to fulfill the HPV requirements have been placed in an Endpoint-specific matrix, and further discussed below. Robust Summaries for each study referenced can be found in Section VI of this Dossier.

A. Chemical/Physical Properties

Table 2. Selected Chemical/Physical Properties of DBPP

Chemical	Boiling Pt. (^{o}C.)	Melting Pt.(^{o} C.)	Vapor Pressure (hPa @ 25 ^{o}C)	Water Solubility (mg/L)	Partition Coefficient (Log Kow)
DBPP CAS No. 2528-36-1	131-132	87.5	0.00933	96 @ 25 ^{o}C.	4.27

All HPV Endpoints for Physical-Chemical Properties have been completed with reliable information, either taken from reputable textbook-references (Table 2), or use of an EPA-endorsed estimation model or from studies conducted specifically to derive this information. The supporting studies, which have been designated as "2-Reliable with restrictions", are included in the Robust Summary section of this Dossier.

In summary, these data indicate that DBPP is a liquid at room temperature and has a low vapor pressure. It has a moderate octanol:water partition coefficient and moderate solubility in water.

Conclusion – Adequate reference values are available to provide needed information on the Physical-Chemical Properties associated with DBPP. Therefore, no additional data development is needed for these HPV Endpoints.

B. Environmental Fate and Biodegradation

Both a Semi-Continuous Activated Sludge (SCAS) test and a River Die-Away test have been conducted with DBPP. While conducted prior to inception of standardized international guidelines for **Biodegradability** testing and GLPs, these studies followed similar standards for conduct subsequently codified into OECD guideline 302 and GLP documentation. They are considered "2-Reliable with restrictions". Both studies have been summarized in the Robust Summary section of this Dossier. The SCAS study has been selected to fulfill this HPV Endpoint and is cited in Table 3 below.

No/little information could be located regarding Photodegradation, Stability in Water (Hydrolysis) and Transport (Fugacity) for DBPP following an extensive literature search. Thus, we have incorporated the use of the estimation models found in EPIWIN (2002) for determination of these HPV Endpoints which have been designated "2-Reliable with restrictions". Estimated **Photodegradation** Rate and **Fugacity** values are cited with the Robust Summaries and also are included in Table 3; thus, these HPV Endpoints are considered complete and each judged as "2-Reliable with restrictions". Limited data is available on Stability of DBPP in Water and the EPIWIN (2002) program is not capable of estimating a hydrolysis value for DBPP. Data available support the conclusion that aqueous hydrolysis of DBPP becomes increasingly important with increasing alkalinity, a characteristic well recognized for other industrial organophosphate chemicals (Mayer, et. al., 1981).

Table 3. Environmental Fate and Biodegradation Parameters for Dibutyl Phenyl Phosphate (DBPP)

Chemical	Biodegradation Rate	Stability in Water (T ½ days @ 25 deg.)	Fugacity (%)	Photodegrad. Rate (T ½)
DBPP CAS No. 2528-36-1	95 %	>100 (pH 5) 57 (pH 7) 10 (pH 9)	Air – 1.21 Water – 40.2 Soil – 55.8 Sediment – 2.8	4.57 hrs-EPIWIN.

The Environmental Fate and Biodegradability of DBPP can be summarized as follows.

If released to the atmosphere, DBPP is expected to rapidly react by photochemically induced hydroxyl radicals, as it has an estimated photodegradation half-life of 4.5 hrs (Table 3 - Photodegradation). Fugacity modeling indicates that DBPP would be expected to precipitate into water and subsequently partition into the soil compartment (Table 3 – Fugacity). In aqueous solution, DBPP is expected to rapidly biodegrade under aerobic conditions primarily due to microbial activity. As with other industrial alkyl, aryl phosphates, it is resistant to hydrolysis in neutral or acid waters (Table 3). Upon further partitioning into the soil compartment (Table 3- Fugacity) DBPP could undergo rapid degradation, especially in a moist, basic soil environment. Like other phosphate esters, DBPP would strongly adsorb to soil particles and much would become soil-bound; thus,

leaching is not an issue. Rapid biodegradation would be the predominant fate process once in the soil compartment. Significant volatilization from soil or water to air is not expected, based on its Vapor Pressure (Table 2). Due to DBPP's modest water solubility and high binding capacity to soil particulate matter, the potential for persistence or bioaccumulation is judged as minimal.

Conclusion – Adequate studies are available to provide needed information for the HPV Designated Environmental Properties associated with DBPP. No further testing is planned.

C. Aquatic Toxicity

Sufficient information is available to characterize the acute toxicity of DBPP to algae, invertebrates and fish. An acute fish study, following OECD test guidance has been conducted on R. trout and is considered "1-Reliable without restriction". A Robust Summary has been prepared for this study and it has been cited in Table 4. Well conducted studies summarizing the effects of DBPP in *D. magna* and Selenastrum algae have been used to fulfill the Acute Invertebrate and Algal Toxicity Endpoints. While not conducted specifically to meet OECD guidelines, both studies used methodology recommended by the US EPA Committee of Methods for Toxicity Testing with Aquatic Organisms (EPA, 1975). These recommendations are consistent with OECD guidelines; the Daphnia study was conducted under GLPs. Hence, these studies have been designated as "2- Reliable with restrictions", selected for development of Robust Summaries, and are cited in Table 4. Two additional aquatic toxicity studies, an Early Life Stage study in R. trout and a Chronic Daphnia study, are included in the Robust Summary section of this dossier, as each study provides additional Supplemental information. Both acute aquatic studies (fish and daphnia) reported LC50/EC50 values in the 2.0 ppm range. Results of these chronic studies are consistent with the level of acute toxicity reported and further support use of the acute studies for HPV purposes.

Table 4. Aquatic toxicity parameters for Dibutyl Phenyl Phosphate (DBPP)

Chemical	Fish LC 50 (mg/L)	Invertebrate EC50 (mg/L)	Algae EC50 (mg/L)
DBPP CAS No. 2528-36-1	2.7 (R. trout)	2.3 (D. magna)	5.4 (Selenastum)

Conclusion – An adequate study is available to meet each of the three Acute Aquatic Toxicity Endpoints for DBPP. No additional testing is necessary for this completed HPV Endpoint category.

D. Mammalian Toxicity Endpoints

A summary of toxicity data used to fulfill the HPV Endpoints for Mammalian Toxicity is found in Table 5. Each report citation has been further summarized in the Robust Summary section of this Dossier.

Table 5. Mammalian Toxicity of Dibutyl Phenyl Phosphate (DBPP)

Chemical	Acute Oral LD50 (rat)	Repeat Dose Toxicity	Ames Test	Chromosomal Aberrations	Reproductive Toxicity
DBPP CAS No. 2528-36-1	2,620 mg/kg	(91-day Rat oral) NOEL = 5 mg/kg/d	Non-mutagenic TA 1535, 1537, 1538, 98, 100 with and w/out S9	(in vivo rat bone marrow) Non-mutagenic	(2-Gen. rat) NOEL = 5 mg/kg/d

1.0 Acute Toxicity

Results of an acute oral toxicity study with DBPP fulfills the HPV Acute Toxicity Endpoint. While conducted prior to OECD Test Guidelines and GLP guidance, its study design is generally consistent with present testing guidance and provides sufficiently reliable, documented information to be classified as "2- Reliable with restrictions".

Thus, DBPP is considered to be slightly toxic after administration by acute oral dosing.

Conclusion – A study of sufficient quality is available to assess the Acute hazard associated with DBPP. Therefore, no additional data development is needed for the Acute Toxicity HPV Endpoint.

2.0 Repeated Dose Toxicity

DBPP has been adequately tested in a subchronic rodent study to define its Repeated Dose toxicity. This study is cited in Table 5 and summarizes a 91-day subchronic rat study by the oral route. This study was conducted using a study design according to OECD Test Guideline 408, and conducted under GLP auspices. Hence, it is considered "1- Reliable without restriction". In all cases, no evidence of an effect on the male or female reproductive organs (including testes) was observed. Urinary bladder and liver proved to be microscopically derived target tissues. The Urinary bladder effects seen are considered related to the Tributyl Phosphate (TBP), in as much as the pathological lesions reported in this study have been seen with TBP (Cascieri et al. 1985; Laham et al, 1985); TBP accounts for approximately 15 % of commercial DBPP. Statistically significant, but generally slight, inhibition of cholinesterase appeared to be of a subclinical nature, as no classical signs of cholinesterase inhibition were observed in rats

from this study; similarly, no classical signs of cholinesterase inhibition were observed in other repeated dose studies (2-Gen. reproductive toxicity study, reported later) or in the acute oral toxicity study previously described. No gross, organ weight/ratio (testes only) or microscopic effects were observed in the ovaries or testes/epididymides or in central/peripheral nerves at any dose level in this study.

Conclusion - The Repeated Dose HPV Endpoint for DBPP has been fulfilled with a well-conducted and documented 91-Day Subchronic study in rats deemed "1-Reliable without restriction". No further testing is needed for completion of information related to the Repeat Dose HPV Endpoint.

3.0 Mutagenicity and Chromosomal Aberrations

3.1 Ames/Point Mutation Testing

When tested in the standard Ames assay for point mutations, DBPP elicited no mutagenic response in any of the *S. Typhimurium* tester strains employed, either with or without inclusion of metabolic activation (Table 5). This study has been classified as "2-Reliable with restrictions" due to its use of fewer replications than recommended in OECD study guide # 471. However, an additional Ames assay (Zeiger et al, 1985), conducted on behalf of the NCI/NTP program, validates the lack of mutagenicity seen in the Ames test with DBPP. The Zeiger et al study is also summarized in the Robust Summary section of this Dossier and referenced in Table 5.

Thus, it is concluded that adequate testing of sufficient quality has been performed on DBPP to evaluate the Ames Test (Point Mutation) HPV requirement; no further testing is needed for this Endpoint.

3.2 - Chromosomal Aberrations

DBPP has been tested *in vivo* for induction of Chromosomal Aberrations in rat bone marrow cells. This study followed OECD Guideline # 475 and was conducted following GLPs. Thus this study is considered as "1-Reliable without restriction". No mutagenic activity was observed with DBPP.

The HPV Chromosomal Aberration Endpoint for testing of DBPP has, thus, been fulfilled with an adequately conducted and documented *in vivo* study; thus, no further testing is needed.

4.0 Reproductive Toxicity

Of direct relevance to completion of the Reproductive Toxicity Endpoint for this HPV assessment with DBPP, is identification of a well documented 2-Generation rat reproduction toxicity study conducted according to OECD Guideline 416. This study has been assessed as "1- Reliable without restriction". It has been summarized in the Robust Summary section of this Dossier and is included in Table 5.

No evidence of morphological effects of either male or female reproductive organs was observed following subchronic DBPP testing (Table 5), nor was there any increase in organ weights or weight ratios of testes/epididymides after subchronic, repeated dose testing.

I**n conclusion, the Reproductive Toxicity HPV Endpoint has been fulfilled using a well documented and conducted 2-Generation reproductive study which has been assessed as "1- Reliable without restriction". Thus, the data requirements for this HPV Endpoint have been met and no further testing is required.**

V. REFERENCES

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VI ROBUST STUDY SUMMARIES -

A IUCLID Data Set for DBPP is Appended